

REMARKS

This Amendment is submitted in response to a non-final Office Action mailed on December 16, 2009. Claims 12-26 are currently pending with claims 21-26 being withdrawn by the Examiner as allegedly belonging to a non-elected invention. Claims 12-20 stand rejected under 35 U.S.C. §112, second paragraph, and claims 12-20 stand rejected under 35 U.S.C. §103(a). In regard to these rejections, Applicants have amended claims 12, 15 and 17. Applicants submit that the amendments to the claims do not introduce any new matter. The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing. In view of the aforementioned amendments and following arguments, Applicants respectfully submit that the rejections should be withdrawn.

In the Office Action, claims 12-20 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner alleged that it is uncertain if the recitation "two partial sequences thereof" suggests that the single stranded target nucleic acid is cleaved at certain points along the single strand of target nucleic acid or modified in some matter to produce the "partial sequence" or if Applicant is suggesting something entirely different (Office Action at page 3).

Without acquiescing to the merits of the Examiner's rejection, and solely to expedite prosecution of the instant application, Applicants have amended claim 12 (from which claims 13-20 depend) to recite that the single-stranded target nucleic acid comprises "a sequence of bases that includes the target base composed of one or more continuous bases and two partial sequences of bases with the target base there between." As amended claim 12 clearly indicates that the single-stranded target nucleic acid is a single contiguous string of bases that comprises two partial sequences, each of which straddles the target base. Accordingly, Applicants respectfully request that the rejection of claims 12-20 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

In the Office Action, claims 12, 13, 14 and 18 were rejected under §103(a) as being unpatentable over Bao *et al.* (U.S. Patent Application Publication No. 2003/0129611) ("*Bao*") in view of Yoshimoto *et al.* (Chemical Communication, Issue 24, pages 2960-2961, October 2003) ("*Yoshimoto*"). In particular, the Examiner alleged that it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to modify the

method of *Bao* to encompass the use of a receptor having hydrogen bonding characteristics to detect the gene mutation in the target nucleic acid rather than the donor and acceptor molecule beacons which result s in FRET as taught by *Bao* to alleviate some of the disadvantage of the FRET system and improve gene mutation detection (Office Action at pages 6-7). Applicants respectfully traverse this rejection for at least the reasons as set forth below.

To establish *prima facie* obviousness under 35 U.S.C. §103, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). This principle of U.S. law regarding obviousness was not altered by the recent Supreme Court holding in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 USPQ2d 1385 (2007). In *KSR*, the Supreme Court stated that “Section 103 forbids issuance of a patent when ‘the differences between the subject matter sought to be patented and the prior art are such the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.’” *KSR Int’l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1734, 82 USPQ2d 1385, 1391 (2007).

The question of obviousness is resolved on the basis of underlying factual determinations including (1) the scope and content of the prior art, (2) any differences between the claimed subject matter and the prior art, (3) the level of skill in the art. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). See also *KSR*, 127 S.Ct. at 1734, 82 USPQ2d at 1391 (“While the sequence of these questions might be reordered in any particular case, the [Graham] factors continue to define the inquiry that controls.”) The Court in *Graham* noted that evidence of secondary considerations, such as commercial success, long felt but unsolved needs, failure of others, etc., “might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.” 383 U.S. at 18, 148 USPQ at 467. Furthermore, the Court in *KSR* took the opportunity to reiterate a second long-standing principle of U.S. law: that a holding of obviousness requires the fact finder (here, the Examiner), to make explicit the analysis supporting a rejection under 35 U.S.C. 103, stating that “rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *Id.* at 1740-41, 82 USPQ2d at 1396 (citing *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). The Supreme Court in *KSR* stated that “a court *must* ask whether the improvement *is more than* the predictable use of prior art elements according to their established functions.” *KSR*

at 1740 (emphasis added). As such, in addition to showing that all elements of a claim were known in the prior art and that one of skill had a reason to combine them, the Office must also provide evidence that a reasonable expectation of success existed. MPEP 2143.02.

While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation (“TSM”) test in an obviousness inquiry, the Court acknowledged the importance of identifying “a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does” in an obviousness determination. *KSR*, 127 S. Ct. at 1731. The Court indicated that there is no necessary inconsistency between the idea underlying the TSM test and the Graham analysis.” *Id.* As long as the test is not applied as a “rigid and mandatory” formula, that test can provide “helpful insight” to an obviousness inquiry. *Id.* “Thus, in cases involving new compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.” *Takeda v. Alphapharm*.

The mere fact that prior art may be modified to produce the claimed product does not make the modification obvious unless the prior art suggests the desirability of the modification. *In re Fritch*, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992); *see, also, In re Papesh*, 315 F.2d 381, 137 U.S.P.Q. 43 (CCPA 1963). In addition, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

As a first matter, Applicants point out that the Examiner has incorrectly interpreted the teaching of *Bao*. In particular, the Examiner states that *Bao* teaches a method for detecting a gene mutation where SEQ ID NO: 11 and SEQ ID NO: 12 represent two single stranded nucleic acids complementary to two partial sequences with a target base and that SEQ ID NO: 10 represents the target sequence having a mutation between SEQ ID NOS: 11 and 12. Such an interpretation of *Bao* is incorrect. Notably, *Bao* does not provide that a mutation resides between SEQ ID NOS: 11 and 12. Rather, it is clear from paragraphs 202, 207 and Table 5 of *Bao* that the molecular beacon probes are designed such that they comprise a nucleotide that is complementary to a mutation in the target sequence. Thus, a mutation in *Bao* is detected by the hybridization of a beacon probe to the mutated target sequence and the subsequent detection of

fluorescent or luminescent energy transfer. As such, *Bao* does not teach the detection of a mutation located in a gap part formed by two single-stranded detecting nucleic acids.

Moreover, according to the disclosure of *Bao*, the effect of fluorescent or luminescent energy transfer is improved by fixing a relative distance between the donor and acceptor beacons. Thus, *Bao* differs from the claimed invention because it does not provide for the formation of a gap part in between both the donor and acceptor beacons at a position opposed to a target base. Rather, *Bao* provides that the detection of a target nucleic acid is dependent upon the distance between the donor and acceptor molecular beacons, which may be adjusted by either removing a guanine residue or adding one to two thymine residues between the positions where the donor and acceptor molecular beacons hybridize to the target nucleic acid. As such, the spacing between the two molecular beacons may be adjusted to affect the resonance energy transfer – and thus the strength of the detectable signal. In contrast, the instant claims do not require the addition or removal of bases located between the position where the detecting nucleic acids hybridize to the partial sequences of bases on the target nucleic acid. Therefore, the instant invention provides for the rapid and inexpensive detection of a gene mutation, since unlike *Bao*, it is not necessary to modify the detecting nucleic acids (molecular beacons) to comprise a fluorescent or luminescent material and/or modify the target nucleic acid to comprise an appropriate spacing between the positions where the detecting nucleic acids hybridize to the target nucleic acid.

Applicants respectfully submit that *Bao* taken singly or in combination with *Yoshimoto* fails to teach and/or suggest the claimed invention. In particular, *Bao* does not teach the detection of a mutation located in a gap part formed by two single-stranded detecting nucleic acids. *Yoshimoto* does not remedy this deficiency of *Bao*. Given that *Bao* and *Yoshimoto* fails to teach or suggest forming a gap part at a position opposed to a target base by forming a double-stranded nucleic acid, forming a hydrogen bond from the target base and a receptor by inserting the receptor having hydrogen bonding characteristics into the gap part, and identifying the gene mutation where the receptor bonds to the target base, they cannot obviate the instant claims. Accordingly, Applicants respectfully request that the rejection of claims 12, 13, 14 and 18 under §103(a) be reconsidered and withdrawn.

In the Office Action, claims 15-17 and 19-20 were rejected under §103(a) as being unpatentable over *Bao* in view of *Yoshimoto* as applied to claims 1-14 and 18 above, and further

in view of Nakatani *et al.* (J. Am. Chem. Soc. (2001) 123:12650-12657) ("*Nakatani*"). In particular, the Examiner alleged that it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to practice the method of *Nakatani* in the method of *Bao* in view of *Yoshimoto* (Office Action at page 11). Applicants respectfully traverse this rejection for at least the reasons as set forth below.


Applicants respectfully submit that for the same reasons as set forth above, *Bao* does not teach the detection of a mutation located in a gap part formed by two single-stranded detecting nucleic acids. Given that this deficiency is not remedied by either of *Yoshimoto* or *Nakatani*, they cannot obviate the instant claims. Accordingly, Applicants respectfully request that the rejection of claims 15-17 and 19-20 under §103(a) be reconsidered and withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims which could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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